REMARKS

Rejection of Claims 1-5, 12-13, and 26-29 Under 35 U.S.C. 103(a)

Claims 1-5, 12-13, and 26-29 stand rejected under 35 U.S.C. 103(a) as being obvious over WO 95/07994 ("Dubensky"), in view of Hu et al. AIDS Res. Hum. Retrovir., Vol. 7(7), 615-620 ("Hu").

Dubensky is cited as teaching replication competent and incompetent alphavirus vectors to express antigen and induce an antigen-specific response. Office Action at page 5. Dubensky is also cited as teaching priming and boosting with multiple administrations using the same vector. *Id.* Hu is cited as teaching boosting "a live recombinant virus immunization with the immunizing protein itself instead of with a second immunization with the recombinant virus." Office Action at pages 5-6. The Patent Office maintains at page 6 that "it would have been *prima facie* obvious to the skilled artisan to utilize the prime boost approach taught by Hu et al in the immunization method of Dubensky et al" and that "based on the state of the art in generating immune responses using replicating and non-replicating viruses, the skilled artisan would have had a reasonable expectation of success in generating an immune response." *Id.*

Applicants respectfully traverse the rejection.

Establishing a *prima facie* case of obviousness by modifying or combining the prior art requires a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986). The skilled artisan reading Hu and Dubensky could not have had a reasonable expectation of success in extrapolating from a DNA-based Vaccinia vector to an RNA-based alphavirus vector. DNA-based viruses that propagate induce different immune responses than RNA-based viruses. RNA-based viruses replicate differently,

have different effects upon the cell, and thus cause different immune responses. Declaration of Dr. Klimstra at ¶4.[1] Because of these differences, "one skilled in the art would have assumed that host responses to RNA viruses versus DNA viruses would be different and therefore not comparable." *Id.* Indeed, the Office Action makes no attempt to address the difference between RNA viruses versus DNA viruses.

There could have been no reasonable expectation of success in extrapolating from Hu and Dubensky to Applicants' claimed subject matter. As Dr. Klimstra notes at paragraph 5, the idea of using prime and boost with an RNA-based vector may appear simple but the skilled artisan would have recognized at the time of filing that differences across viral species means that the cited art does not provide a reasonable expectation of success.

Applicants therefore respectfully request withdrawal of the rejection.

Respectfully submitted,
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[1] Sánchez-Puig JM et al., "Susceptibility of different leukocyte cell types to Vaccinia virus infection," Virol J. 2004 Nov 22;1:10, and Yu et al., "Comparative analysis of tropism between canarypox (ALVAC) and vaccinia viruses reveals a more restricted and preferential tropism of ALVAC for human cells of the monocytic lineage," Vaccine. 2006 Sep 29;24(40-41):6376-91, cited by Dr. Klimstra in his declaration, are enclosed as Exhibit 1 and 2, respectively.